

Claims:

1. A method of treating a central nervous system (CNS) lymphoma comprising the step of administering a therapeutically effective amount of an anti-CD20 antibody or fragment thereof.
2. A method to treat or prevent meningeal relapse in a subject with lymphoma comprising the step of administering a therapeutically effective amount of an anti-CD20 antibody or fragment thereof.
3. The method of claim 1, wherein the CNS lymphoma is selected from the group consisting of: primary CNS lymphoma, (PCNSL) leptomeningeal metastasises (LM), or Hodgkin's Disease with CNS involvement.
4. The method of claim 3, wherein the CNS lymphoma is LM and wherein the anti-CD20 antibody or fragment thereof is administered in combination with cytarabine and thiotepa or methotrexate and <sup>111</sup>In-diethylenetriamine pentaacetic acid.
5. The method of claim 1, wherein the anti-CD20 antibody fragment is selected from the group consisting of Fab, Fab' and F(ab')<sub>2</sub>.
6. The method of claim 2, wherein the anti-CD20 antibody fragment is selected from the group consisting of Fab, Fab' and F(ab')<sub>2</sub>.
7. The method of claim 1, wherein the anti-CD20 antibody is a human antibody, humanized, bispecific or chimeric.
8. The method of claim 2, wherein the anti-CD20 antibody is a human antibody, humanized, bispecific or chimeric.

9. The method of claim 1, wherein the anti-CD20 is Rituximab or IF5.

10. The method of claim 2, wherein the anti-CD20 is Rituximab or IF5.

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11. The method of claim 9, wherein the anti-CD20 antibody is Rituximab and is administered to the subject in a dosage of about 10 mg to about 375 mg/M<sup>2</sup> per week for four weeks.

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12. The method of claim 11, wherein the anti-CD20 antibody is Rituximab and is administered to the subject in a dosage of about 10 mg to about 375 mg/M<sup>2</sup> per week for four weeks.

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13. The method of claim 1, wherein the anti-CD20 antibody is administered intrathecally or intraventrically.

14. The method of claim 2, wherein the anti-CD20 antibody is administered intrathecally or intraventrically.

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15. The method of claim 1, wherein the anti-CD20 antibody is administered in combination with methotrexate, CHOP, CHOD cytarabine, leucovorin, thiotepa and vincristine or combinations thereof.

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16. The method of claim 2, wherein the anti-CD20 antibody is administered in combination with methotrexate, CHOP, CHOD cytarabine, leucovorin, thiotepa and vincristine or combinations thereof.

17. The method of claim 1, wherein the anti-CD20 antibody is administered prior to whole brain irradiation.

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18. The method of claim 1, wherein the anti-CD20 antibody is Rituximab and is administered intrathecally with methotrexate.

19. The method of claim 1, wherein the anti-CD20 antibody is Rituximab  
5 and the antibody is labeled.

20. The method of claim 19, wherein Rituximab is labeled with an isotope selected from the group consisting of:  $^{211}\text{At}$ ,  $^{212}\text{Bi}$ ,  $^{67}\text{Cu}$ ,  $^{123}\text{I}$ ,  $^{131}\text{I}$ ,  $^{111}\text{In}$ ,  $^{32}\text{P}$ ,  $^{212}\text{Pb}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{153}\text{Sm}$ ,  $^{99\text{m}}\text{Tc}$ , and  $^{90}\text{Y}$  and is administered in a  
10 radioimmunotherapeutically effective amount.

21. The method of claim 20, wherein the radioimmunotherapeutically effective amount provides irradiation at a dose in the range of about 10 to about 200 cGy to the whole body of the patient.  
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22. The method of claim 22, wherein the anti-CD20 antibody is administered in combination with an anti-CD40 antibody or an agent which inhibits interaction of CD40 with CD40L.

23. The method of claim 22, wherein the anti-CD20 antibody is administered in a pharmaceutically acceptable dosage of the antibody ranging from about 0.001 to about 30 mg/kg of human body weight.  
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24. The method of claim 23, wherein the anti-CD20 antibody is administered in a pharmaceutically acceptable dosage of the antibody ranging from about 0.01 to about 25 mg/kg human body weight.  
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25. The composition of claim 24, wherein the anti-CD20 antibody is administered in a pharmaceutically acceptable dosage of the antibody ranging from about 0.4 to about 20.0 mg/kg human body weight.  
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26. A method of diagnosing PCNSL in a subject comprising the steps of:  
(A) administering to said subject an anti-CD20 antibody or anti-CD20  
antibody fragment bound to a detectable label; and  
5 (B) detecting the localization of said label.

27. The method of claim 26, wherein the detectable label is:  $^{211}\text{At}$ ,  $^{212}\text{Bi}$ ,  
 $^{67}\text{Cu}$ ,  $^{123}\text{I}$ ,  $^{131}\text{I}$ ,  $^{111}\text{In}$ ,  $^{32}\text{P}$ ,  $^{212}\text{Pb}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{153}\text{Sm}$ ,  $^{99\text{m}}\text{Tc}$ , or  $^{90}\text{Y}$ .

- 10 28. The method of claim 26, wherein the anti-CD20 antibody is  
Rituximab.

29. The method of claim 1, wherein the anti-CD20 antibody is linked to a  
brain blood barrier (BBB) permeability enhancing agent.

- 15 30. The method of claim 29, wherein the BBB permeability enhancing  
agent is OX-26, B3/25, Tf6/14, OKT-9, L5.1, 5E-9, RI7 217 or T58/30.

31. The method of claim 1, wherein the anti-CD20 antibody further  
20 comprises a lipophilic vector or an immunolipophilic vector.

32. The method of claim 31, wherein the lipophilic vector is procarbazine,  
an omega-3 fatty acid, a diacyl glycerol, a diacyl phospholipid, a lyso-phospholipid,  
cholesterol or a steroid.

- 25 33. The method of claim 1, further comprising the step of administering an  
anti-B cell antibody or fragment thereof in combination with the anti-CD20 antibody  
or fragment thereof.

34. The method of claim 33, wherein the anti-B cell antibody is anti-CD19 antibody or fragments thereof, anti-CD22 antibody or fragments thereof, anti-CD38 antibody or fragments thereof, or anti-major histocompatibility complex (MHC) II antibody or fragments thereof.

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35. A composition for the treatment of CNS lymphoma for intrathecal administration comprising an anti-CD20 antibody and an anti-B cell antibody wherein the antibodies are administered at a dosage ranging from about 0.4 to about 20.0 mg/kg human body weight.

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36. A method of treating a central nervous system (CNS) lymphoma comprising intrathecally administering a therapeutically effective amount of an antibody or antibody fragment that binds to a B cell antigen.

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37. The method of claim 36 wherein said antigen is selected from the group consisting of CD10, CD14, CD20, CD21, CD22, CD23, CD24, CD37, CD53, CD72, CD73, CD74, CD75, CD76, CD77, CD78, CD79a, CD79b, CD80, CD81, CD82, CD83, CDw84, CD85 and CD86.

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38. The method of claim 36 wherein said antibody is a B cell depleting antibody.

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39. The method of claim 36 wherein said antibody or antibody fragment is conjugated to a toxin.

40. The method of claim 36 wherein said antibody or antibody fragment is conjugated to a drug.

41. The method of claim 36 wherein said antibody or antibody fragment is conjugated to an enzyme.

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42. The method of claim 36 wherein said antibody or antibody fragment is conjugated to a radionuclide.

5 43. The method of claim 36 wherein said antibody or antibody fragment is administered in combination with at least one chemotherapeutic.

44. The method of claim 43 wherein said chemotherapeutic is selected from the group consisting of thiotepa, cyclophosphamide, busulfan, improsulfan,  
10 piposulfan, benzodopa, carboquone, meturedopa, uredopa, altretamine, triethylenemelamine, trietylenephosphoramide, triethylenethiophosphaoramide, trimethylolomelamine, chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembiehin, phenesterine, prednimustine, trofosfamide, uracil mustard,  
15 carmustine, chlorozotocin, fotemustine, lomustine, nimustine, ranimustine, aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, calicheamicin, carabycin, carminomycin, carzinophilin, chromoinycins, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin, epirubicin, esorubicin, idambicin, marcellomycin, mitomycin, mycophenolic acid, nogalamycin,  
20 olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin, methotrexate, 5-fluorouracil (5-FU), denopterin, methotrexate, pteropterin, trimetrexate, fludarabine, 6-mercaptopurine, thiamiprine, thioguanine, ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, 5-FU,  
25 calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone, aminoglutethimide, mitotane, trilostane, frolic acid, aceglatone, aldophosphamide glycoside, aminolevulinic acid, amsacrine, bestabucil, bisantrene, edatraxate, defofamine, demecolcine, diaziquone, elfornithine, elliptinium acetate, etoglucid, gallium nitrate, hydroxyurea, lentinan, lonidamine, mitoguazone, mitoxantrone,  
30 mopidamol, nitracrine, pentostatin, phenamet, pirarubicin, podophyllinic acid,

2-ethylhydrazide, procarbazine, razoxane, sizofran, spirogermanium, tenuazonic acid, triaziquone, 2, 2',2''-trichlorotriethylamine, urethan, vindesine, dacarbazine, mannomustine, mitobronitol, mitolactol, pipobroman, gacytosine, arabinoside, cyclophosphamide, thiotepa, paclitaxel, doxetaxel, chlorambucil, gemcitabine, 5 6-thioguanine, mercaptopurine, methotrexate, cisplatin, carboplatin, vinblastine, platinum, etoposide (VP-16), ifosfamide, mitomycin C, mitoxantrone, vincristine, vinorelbine, navelbine, novantrone, teniposide, daunomycin, aminopterin, xeloda, ibandronate, topoisomerase inhibitor, difluoromethylornithine (DMFO), retinoic acid, esperamicins, capecitabine, tamoxifen, raloxifene, aromatase inhibiting 10 4(5)-imidazoles, 4 hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, toremifene, flutamide, nilutamide, bicalutamide, leuprolide, goserelin; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

45. The method of claim 36 wherein said antibody or antibody fragment is 15 specific to a B cell antigen selected from the group consisting of CD19, CD20, CD21, CD22, CD37 and CD40.

46. The method of claim 45 wherein said antibody or antibody fragment is 20 RITUXAN® and said method of treatment further comprises administration of a cytokine.

47. The method of claim 46 wherein said cytokine is IL-10.

48. The method of claim 36 which comprises administration of a depleting 25 anti-CD20 antibody and a CD40L antagonist.

49. The method of claim 48 wherein said CD40L antagonist is an antibody that specifically binds CD40L.

50. The method of claim 36 wherein a radiolabeled antibody to CD20 is administered.